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Potency of Δ9–Tetrahydrocannabinol and Other Cannabinoids in Cannabis in England in 2016: Implications for Public Health and Pharmacology

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Keywords:	herbal cannabis, sinsemilla, resin, potency, cannabinoid, delta-9-tetrahydrocannabinol, cannabidiol, cannabinol
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Potency of Δ^9–Tetrahydrocannabinol and Other Cannabinoids in Cannabis in England in 2016: Implications for Public Health and Pharmacology

Short title: Potency of Δ^9–THC and Other Cannabinoids in Cannabis in England in 2016

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Conflicts of interest and financial disclosures

David Potter, Kathy Hammond, and Shaun Tuffnell are employed by GW Pharmaceuticals group companies and are shareholders in GW Pharmaceuticals plc, a public company that is researching and developing a portfolio of cannabinoid medicines.

Christopher Walker is employed by the Drug Control Centre, Kings College London.

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ABSTRACT

Background: In 2005 and 2008, studies reported that cannabis in England had become dominated by the sinsemilla (unseeded female) form. The average potency (Δ9-tetrahydrocannabinol [THC]

content) of this material had doubled over the previous decade. Cannabis resin then circulating contained approximately equal ratios of THC and cannabidiol (CBD), whereas sinsemilla was almost devoid of CBD. Despite raised health concerns regarding sinsemilla use and the development of psychotic disorders, no update on street cannabis potency has been published since 2008. **Methods:** A total of 995 seized cannabis samples were acquired from the same five constabulary areas included in the 2005 study. The differing forms were segregated and a representative 460 samples analyzed to assess their cannabinoid content using gas chromatography. **Results:** The resultant median sinsemilla potency of 14.2% THC was similar to that observed in 2005 (13.9%). In each case, sinsemilla contained minimal CBD. Compared with 2005, resin had significantly higher mean THC (6.3%) and lower CBD (2.3%) contents ($p < 0.0001$). **Conclusions**: Although the average THC concentration in sinsemilla samples across the five constabularies has remained stable since 2005, the availability of this potent form of cannabis has further increased. Moreover, the now rarer resin samples show significantly decreased CBD contents and CBD:THC ratios, leaving the United Kingdom's cannabis street market populated by high-potency varieties of cannabis, which may have concerning implications for public health.

KEYWORDS: herbal cannabis, sinsemilla, resin, potency, cannabinoid, Δ^9-tetrahydrocannabinol, psychosis, cannabidiol, cannabinol

INTRODUCTION

In all European countries, across all age groups, cannabis is the most popular illicit drug. The prevalence of cannabis use in Europe is approximately five times that of other substances. Home Office data indicate that, in England and Wales, cannabis remains the most commonly used illicit drug, where it accounted for 109,527 of the 148,553 drug samples seized by police in the financial year ending March 2016.[1]

Many studies have reported the consistent and dose-dependent association between cannabis use and increased risk of developing a psychotic disorder.[2-6] In their 2006 World Drug Report, the United Nations Office on Drugs and Crime emphasized the global nature of this problem in a detailed chapter titled, "Cannabis: Why We Should Care."[7] The European Monitoring Centre on Drugs and Drug Addiction (EMCDDA) reported that overall, the number of first-time treatment entrants for cannabis problems increased from 45,000 in 2006 to 69,000 in 2014. The causes of the increase in the number of treatment entrants are unclear, but they may be linked to changes in the prevalence of intensive cannabis use and other factors such as the availability of more harmful and higher potency products.[8]

Within the United Kingdom (UK), the illicit drug commonly exists as either a resin (more commonly called *hashish* in the United States) or as dry herbal material. The resin is made by a range of cultural

methods that physically remove and collect the trichomes from the plant. This process in turn produces materials of varying color and texture. There are two distinct types of dry herbal material. One form is imported into the UK from more southerly countries and contains floral and foliar material from outdoor-grown pollinated female plants. This form is commonly referred to as *traditional herbal cannabis* in the UK and as *marijuana* in the United States. The more frequent type of dried-plant material in the UK consists of unpollinated female floral tissue only. It is usually more potent and is referred to in this article using the widely used term *sinsemilla* (a Spanish derivation meaning "without seeds"). It is also known by a vast range of colloquial names. This form can be grown outdoors in more southerly regions but is predominantly grown in more secure indoor locations, in the absence of male plants, using highly technical equipment.

A study of cannabis potency in England in 2005 indicated that sinsemilla potency (i.e., Δ^9-tetrahydrocannabinol [THC] content) had doubled over the previous 10 years. The same study indicated that low-potency cannabis resin no longer dominated the market. Resin was found to contain THC and cannabidiol (CBD) in varying ratios (averaging approximately 1:1), whereas herbal cannabis products almost totally lacked CBD. As CBD has antipsychotic properties that can moderate the effects of THC, the combined shift in use from low-potency resin with CBD to high-potency, intensively grown cannabis lacking CBD suggested that the illicit cannabis now circulating was potentially more harmful than that in use hitherto.[9,10] A Home Office survey of UK illicit cannabis potency was performed 3 years later on the recommendation of the Medicines & Healthcare Products Regulatory Agency (MHRA); it showed that the upward trend in THC content had continued, as had the decline in availability of cannabis resin.[11]

The EMCDDA in 2016 dedicated an entire section to the changes in cannabis potency across the European Union, reporting that cannabis grown in Morocco, the long-term main source of resin used in the UK and Spain, has changed significantly in recent years. Plant varieties with a higher THC content now are now being grown to provide more potent cannabis products to meet the taste of European users.[12] As a result, resin potency has increased in France in recent years,[13] and resin elsewhere in Europe may have followed the same trend.

The illicit use of cannabis is primarily for recreational purposes, but in 1997 and 1998, the British Medical Association[14] and House of Lords Science and Technology Committee[15] respectively highlighted the common use of illicit cannabis in the UK for medicinal reasons. No legal forms of cannabis plant-based medicine then existed. The MHRA has since approved the UK use of the medicine Sativex®, containing THC and CBD, to treat spasticity symptoms in multiple sclerosis patients for whom other treatments have failed.[16] However, the National Institute for Health and Care Excellence has not authorized it in England as a prescription medicine, funded by the National Health Service.[17]

In the absence of prescription cannabis-based medicines, the use of illicit cannabis for medicinal purposes continues in the UK,[18] with one survey suggesting that 72% of users acquire the substance from "dealers."[19] Although often efficacious in the management of chronic pain, spasticity, and other ailments,[18] the quality and safety of these materials is never assured.

In the summary of their 2015 World Drug Report, the United Nations Office on Drugs and Crime stated that:

there is growing evidence that it is time to change the widespread perception of cannabis as an illicit drug without serious health consequences. The current cannabis market is far more complex and sophisticated than in the past and there is a far larger variety of cannabis products on the market than ever before, some of which appear to be more harmful than their predecessors. Highly potent strains of herbal cannabis, such as sinsemilla, which have high THC content (the main psychoactive ingredient) coupled with low CBD content (a cannabinoid with anti-psychotic properties), are becoming increasingly popular in some markets. Given that there is growing evidence of links between cannabis use and some forms of mental illness , these developments may lead to even greater morbidity; an issue worthy of close monitoring.[20]

The mental illness referred to here especially includes the well-established association between cannabis use and psychotic disorders[6] and cognitive deficit.[4]

To address this issue, we investigated how cannabis circulating in England has changed since the previous surveys conducted in 2005 and 2008. The aim of this study was to quantify the relative proportions of sinsemilla, traditional herbal cannabis, and resin being used at the time of police arrest.

In fresh plant material, THC, CBD, and other newly formed cannabinoids exist in the cannabinoid acid forms, such as tetrahydrocannabidiolic acid, or THCA, and cannabidiolic acid, or CBDA. As the plant material ages or is heated (as during gas chromatography [GC]), the acid molecules lose a carboxyl moiety. Decarboxylation results in the conversion of the cannabinoid acids into their neutral forms (e.g., CBDA→CBD). As is common, this article hereafter refers to the cannabinoids in their neutral form only.

METHODS

Acquisition and identification of samples

Assistance was sought from the same five constabularies used in the 2005 study, i.e., Derbyshire, Kent, London Metropolitan, Merseyside, and Sussex. The police were asked to supply any available seized cannabis samples in their property stores. All samples had been seized by police in 2015 (Kent and London Metropolitan) or 2016 (Derbyshire, Merseyside, and Sussex). All had been retained at ambient temperature in police evidence store rooms, in sealed, airtight, tamper-evident bags, for a maximum of 12 months before collection. The materials had been seized from users and suppliers "on the street" or during searches of properties involved in cannabis dealing or consumption. The materials were assessed visually, using a simple light microscope where necessary, and the form of the cannabis sample was established. Mirroring the practice of the Home Office, when recording illicit cannabis seizures, all resin types were grouped together as a single category.[1]

Some samples were accompanied by portable cannabis grinders, used to break herbal cannabis and sinsemilla into a suitably friable texture for smoking. More complex grinders included a fine metal mesh within the construction. Glandular trichomes dislodged from the plant during grinding could fall through this sieve and be collected in a separate chamber within the device. Glandular trichomes are the principal or sole site of cannabinoid biosynthesis.[21] Two grinders were found with sufficient

powder to enable analysis. This material is commonly referred to as *kief* and consists almost entirely of glandular trichome resin heads and stalks.

A total of 995 analyzable cannabis samples were received, 929 of which were sinsemilla. The number of sinsemilla samples available from each constabulary ranged from 81 to 349. To give a balanced picture of the cannabinoid content of these samples across the constabularies, 80 samples were selected at random from each, thereby reducing this number to 400. However, only 6 traditional herbal cannabis materials and 58 resin samples were identified, of which 53 were available in sufficient quantity for analysis. Due to the small numbers of traditional herbal and resin samples available, all were analyzed, along with the powders found in the two herb grinders. While waiting for analysis, all samples were deep frozen at −20°C. Mirroring the practice of the cannabis consumer, no attempt was made to adjust the moisture level of the dry sample.

Previous studies on illicit cannabis potency in the UK have included analyses of hash oil. This liquid preparation is made by dissolving, and subsequently concentrating, cannabis extracts in an organic solvent.[22] More recently, highly potent solid concentrates called butane hash oils (BHO), produced using liquid butane as the solvent, have appeared within the marketplace.[23] No hash oil or BHO samples were identified in seizures by the five constabularies in this study. Many samples seized, were found to be a mixture of cannabis and tobacco. All were excluded from this study. Approximately 1% of the seized samples, labeled by police as Green Vegetable Material, GVM or similar, were not cannabis but were suggested to be so-called “legal highs” consisting of other plant species with added synthetic cannabinoid receptor agonists.

Subsampling and analysis

Herbal cannabis products are extremely inhomogeneous materials, whereas resin samples are substantially more uniform.[24] Experience of analyzing many thousands of cannabis samples at GW Pharmaceuticals supports this view. An analyst would require several subsamples of any one batch of seized material to reliably determine the average potency of that batch. For the cannabis user, this inhomogeneity means that joints made from any one batch of cannabis are likely to vary in potency. In this study, just one replicate from each batch of seized material was analyzed, thereby capturing the same potency variability encountered by users. The size of the subsample in each case was 250 mg, a typical generous weight of cannabis used in a single joint. On the basis of several publications, a report by the EMCDDA stated that, across Europe, typical cannabis contents in a single joint was 100 to 260 mg.[23] Small[25] reported a Europe-wide range of 0.1 to 0.3 g. An accurate overall median potency for cannabis nationwide was achieved in this study by analyzing a large number of separate samples. These were taken at random from each crime scene. Replicating the practice of cannabis users, fibrous branch material often needed to be removed from the sample and discarded. The remaining floral tissue was then weighed and analyzed by GC.

Each 250-mg sample of material was placed in a Corning Centristar 50-mL centrifuge tube, to which was added 20 mL of ethanol (99.7%) and 5 mL of phenanthrene stock solution (10 mg mL^{-1} in ethanol) as an internal standard. The sample was sonicated for 30 minutes and then centrifuged at 4000 rpm for 5 minutes. The extracts were homogenized and transferred to GC vials. Gas chromatographic analyses were performed on an Agilent 7890 GC equipped with an autosampler, a flame ionisation detector, and a Zebron ZB—5HT Inferno (Column, 30 meters in length, 0.32 mm internal diameter, and 0.25-µm film thickness The oven sample preparation program is summarized

in Table 1. The injector and detector temperatures were both 325°C. This process achieved complete decarboxylation of the cannabinoids.

The following instrument parameters were employed. Front injector syringe size 10 µL, injection volume 1 µL. Front inlet hydrogen pressure 7 psi; heater temperature 325°C; split ratio 50:1; total flow 149.5 mL min^{-1}; septum purge flow 3 mL min^{-1}; split flow 143.6 mL min^{-1}. Front detector FID temperature 325°C; hydrogen flow 30 mL min^{-1}; air flow 450 mL min^{-1}; make-up flow 13 mL min^{-1}.

Statistical analyses were performed using SAS 9.3 software, from SAS Institute Inc., Campus Drive, North Carolina 27513.

RESULTS AND DISCUSSION

Relative proportion of sinsemilla, traditional herbal and resin

Annual Home Office reports show that from 1994 to 2000, resin accounted for a steady 70% ± 2% of all illicit cannabis seized in England and Wales. Its dominance in the market then started to decrease.[26] In the five constabularies included in this study, the proportion had fallen to 43% by 2005,[9] to 31% in 2008[11] and then to 6% in this latest analysis. In all three potency surveys, the London Metropolitan area had the lowest proportion of resin among the five constabularies, and perhaps leads a national trend. The precise proportions in each of the individual constabularies are shown in Table 2. The fall in resin proportions was similar in the Home Office 2015 records for England and Wales overall, which showed resin samples to account for 5% of the seized resin and herbal cannabis total.[1]

The London Metropolitan area was also notable in the 2005 study for having the highest proportion of traditional herbal samples. That remained the situation in 2008 and 2015, but in the latter case, occurrences were minimal, i.e. 1.4% of the total samples seized.

Cannabinoid content of sinsemilla

As in the previous studies, THC contents were highly variable, ranging from 1.9% to 22.5%. The median was 14.2%. This finding is similar to that in the same five constabularies in 2004/2005 (13.9%). The distribution of potency values was also very similar, as seen in Figure 1. Some variation was found between the median potencies of the individual constabularies (Derbyshire 13.1%, Kent 12.5%, Sussex 13.3%, London Metropolitan 15.5% and Merseyside 15.8%). In the 2008 Home Office Potency Study, across 23 constabularies, a slightly higher median was recorded: 15.0% THC.

Although samples varied widely in THC content from ≈ 2% to 24%, a large majority (80% of samples) had THC contents within a much narrower range of 10% to 20% THC (Figure 2). Those below 10% were visually re-examined after analysis, where possible. In almost all cases, those recording a %THC of less than 8% gave visible signs that the material was not of the highest potency. Many were found to be residual broken particles left after the bulk of the original deal had been used (sometimes called “shake”). Others were poorly grown and processed materials. In a few cases, materials showed visible signs of decay. This finding suggests that, at the time of packaging, the vast majority of materials were within the 10% and 20% THC range. Had this survey been based on freshly

packaged samples only, as is the case with some other surveys, the median potency would probably have been at least 1% higher.

Unlike other illicit drugs in powder or tablet form, the visual appearance of sinsemilla enables users to at least make an approximate judgement of potency. Although never a reliable way of estimating potency, those observers with the ability to make a close visual assessment of trichome density and color can make an informed judgement.[10]

In a natural setting, cannabis plants exist in three main chemotypes (chemical phenotypes) producing predominantly THC, CBD, or a mixture of the two.[27] Resin has traditionally been made using a mixture of all three chemotypes. However, continual selection of high-THC plants, when breeding and growing for traditional or sinsemilla herbal cannabis, has resulted in CBD being generally absent in these products. None of the 247 sinsemilla samples analyzed in 2004/2005 contained more than 1% CBD. In this latest study, the dominance of THC continued, but one Derbyshire sample was notable for containing 7% THC and 9% CBD. Sinsemilla samples with a mixed THC/CBD profile are to be expected on occasions, especially if sourced from a single plant. In a previous study, when plants were grown from packeted seed of 52 commercial varieties and analyzed, 48 were entirely the THC chemotype, but seeds in the other four occasionally produced plants with the mixed THC/CBD profile. In total, 3% of seeds produced mixed chemotype plants.[28(p 144)] None of the four seed packets stated that plants containing significant CBD might arise. In recent years, commercially available seeds described as having high CBD levels have been advertised, but this availability does not appear to have had a significant effect on the UK illicit cannabis market.

The overall median CBN content of sinsemilla in this latest study was 0.24%. For individual constabularies, the median contents were 0.33% for London Met, 0.29% for Merseyside, and 0.28% for Kent. For Derby and Sussex, the median was below the quantifiable limit of 0.15%.

Cannabinoid content of seeded herbal

The THC contents of the six seeded herbal samples were similar to that previously reported (median [range], 3.5% [1.8%–5.7%]). CBD levels were below the quantifiable limit. As previously reported, CBN levels were much higher than commonly found in sinsemilla (min, 0.9%; max, 2.9%; median, 2.7%). The high CBN content, relative to THC, suggests excessive THC degradation during processing and a lengthy journey to the UK.

Potency of trichome powders in herb grinders

The trichome powders were the most potent samples analyzed in this study, containing 46.0% and 34.3% THC with 0.7% and 0.3% CBN, respectively. A level of 0.2% CBD was detected in the first but the level was below the quantifiable limit in the latter.

Cannabinoid content of resin

Resin samples showed an even wider variation in THC content than that seen with sinsemilla. This finding was accompanied by widely varying CBD and CBN contents. In two samples, no cannabinoids were detected. These were excluded from the statistical analysis. Several others had total measurable cannabinoid contents of less than 1%. In the 2005 study, the maximum THC content observed was 10.8%. In this latest study, a quarter of samples exceeded that value, the most potent exceeding 29% THC. This sample was one of two resin samples seized in a prison, where the high potency facilitated the smuggling of high quantities of THC in minimal volume. One notable street sample contained 11% CBD, but all others contained 6% or less.

The THC:CBD:CBN ratios of individual samples in the 2005 and 2016 studies are compared graphically in Figure 3. These data were analyzed using the Kolmogorov–Smirnov test for different distributions, which showed that the two distribution patterns for 2005 and 2016 were significantly different ($p < 0.0001$). A Wilcoxon Rank-Sum test showed that the mean potency levels in 2016 (6.3% THC) were significantly higher ($p < 0.0001$) than those in 2005 (3.7% THC). Similar significance levels were observed for the drop in mean CBD content from 4.3% to 2.3%. As a consequence, the change in mean THC:CBD ratio from 0.8:1.0 to 2.7:1.0 was also highly significant ($p < 0.0001$). The difference in mean CBN content of resin in 2005 (1.7%) and 2015 (1.3%) was not significant ($p = 0.10$).

Unlike sinsemilla, where visual examination gave some indication of likely cannabinoid content, the appearance of small cannabis resin samples gave minimal indication. This observation is illustrated in Figure 4, which shows a selection of 15 of the samples. Accompanying this, Table 3 shows the %THC, CBD, and CBN of each.

The high THC content of the resin powders in the grinders illustrated the ability of sieving systems to produce potent materials lacking CBD. In the Netherlands, where a significant proportion of cannabis circulating has been purchased legally in regulated coffee shops, much of the resin is so-called "Nederhasj" and contains high levels of THC and minimal levels of CBD. It is made using entirely high-THC chemotype sinsemilla as the starting material.[29] A range of equipment is available to wet or dry sieve cannabis for resin production. The starter material for this process is usually the waste material left when sinsemilla is manicured.[28(p38)] However, sieving devices are reported to have been used in Morocco to produce potent resins.[30] In the UK, it is possible that this sieving is only widespread among producers for personal use.

Only 3 of the 54 samples in this study contained THC and no detectable CBD. This finding suggests that the majority of the resin samples were produced oversees, in locations where CBD-chemotype cannabis are common.

Effect of aging on cannabinoid levels

Mean CBN levels in sinsemilla samples were very low, despite the samples having often aged in police stores for many months before analysis. However, the THC content of resin is reported to be much less stable than that of sinsemilla. Atmospheric exposure of THC causes oxidation to CBN and other degradants. Martone and Della Casa[31] showed that, even when stored in the dark, the half-life

of THC was often less than 1 year, and in some cases, THC had disappeared almost completely within 2 years.

For those samples in this study, where the exact the length of time in police storage was available (n=34), a regression calculation was performed to determine any correlation between the level of CBN formation and the length of time spent in storage prior to the sample being deep frozen. In a scatter plot (not shown), the regression line was almost horizontal, highlighting that no meaningful correlation existed between storage date and the proportion of CBN. The regression model can be summarized as:

CBN as % of THC+CBN total = 0.0109x + 21.257 * Weeks in storage (p = 0.956977, R^2 = 9.24E-05).

Police evidence bags are designed to have an excellent seal, thereby protecting police officers against accusations of tampering with evidence. This design has protected the resin from oxidative degradation. The cannabinoid levels detected are therefore a fair reflection of those existing at the time the samples were seized.

Cannabis concentrates

Two samples of hash oil were provided by constabularies not included within this main study. Both contained 51% THC and less than 1% CBD. A few forms of BHO were provided, described as wax, wax-crumble, or shatter. These contained between 73% and 83% THC, with less than 1% CBD. These analyses are reported here for interest.

Implications for pharmacology

Δ^9–THC is the main ingredient in cannabis affecting perception, mood, emotion, and cognition that together constitute the psychotropic effect.[32] This effect is linked to its interaction with two G protein-coupled receptors named cannabinoid receptor types 1 (CB_1) and 2 (CB_2). CB_1 receptors are found in brain and nerve tissue and their activation can, among other things, beneficially control motor function and induce signs of analgesia. CB_2 receptors are found within the immune cells. Although less well understood, their activation can lead to cytokine release inside and outside the brain.[33] Only four of the many cannabinoids found in cannabis are known to interact with these receptors, viz Δ^9–THC, Δ^8–THC, Δ^9–tetrahydrocannabivarin (i.e., THCV) and CBN. Δ^8–THC was not found in quantifiable amounts in any of the samples in this study, and Δ^9–THCV never exceeded 0.2% w/w. It is unlikely that these two cannabinoids could have majorly affected the pharmacologic activity of the samples. CBN binds less potently to CB_1 and CB_2 receptors than Δ^9–THC, but as it was frequently present in substantial quantities, especially in resin and imported herbal material, it therefore had the potential to impart some pharmacological effect. CBD lacks psychotropic activity but has markedly different therapeutic potential to Δ^9–THC, offering potential management of inflammation, anxiety, emesis, and nausea. It also offers neuroprotective and antioxidant activity.[33]

In all but one case, the 400 sinsemilla samples were devoid of CBD, as were the few imported herbal samples, and they therefore lacked the pharmacologic qualities that this ingredient might otherwise offer. Due to its antipsychotic activity, CBD also has the potential to reduce the onset or degree of the psychoactive effects of THC.[23]

CBD was present in resin samples, but in widely varying ratios with THC. This finding would be expected to greatly affect the range of medical conditions that might benefit from cannabis administration, as well as the magnitude of effect. This predicted variability in efficacy of THC+CBD mixtures is exacerbated by evidence that THC and CBD act together synergistically.[34] When drugs demonstrate synergy, even small variations in ingredient ratio can have a relatively large effect on overall activity.

CBN is a degradant of THC and is less pharmacologically active. Its presence therefore indicates that THC and overall activity may have been reduced. In some cases, however, the loss of THC will have beneficially reduced the potential for psychoactive effects while, at the same time, increasing the CBD:THC ratio.

Due to the reduction in relative availability of resin compared with sinsemilla since the last cannabis potency studies, the overall proportion of CBD within the available cannabis market has been significantly reduced. Much of the efficacy and protection from some of the adverse effects of THC has been lost.

Licenced medicines in the Western world are expected to meet specified levels of quality, safety, and efficacy. Apart from highlighting the variable protection from psychoactive adverse effects, this article does not address the safety issues but acknowledges that microbial, pesticide, and heavy metal residues as well as adulterants are frequently present in herbal products where quality has not been managed.

Implications for mental health

Rising THC levels and disappearing CBD levels have the potential to impact the number of cannabis users at risk of developing psychotic disorders.[35] Consistently, epidemiological evidence has shown that the strength of the association between cannabis use and the increased risk of psychotic disorder is dose-response related. High-potency cannabis carries the greatest risk.[35] Moreover, several experimental studies demonstrated that the administration of tetrahydrocannabinol, the active ingredient of cannabis, can induce transient psychosis in healthy volunteers and this effect can be dampened by coadministration of cannabidiol.[36]

More recently, clear evidence has shown that the risk of developing a psychotic disorder or experiencing psychotic symptoms after cannabis use is related to: (1) the THC content of the cannabis, and (2) a THC:CBD ratio in that cannabis of >1. [35, 37] Moreover, the use of types of cannabis with a THC:CBD ratio of ≤1 is not associated with an increase in the risk of psychosis.[35]

Although we reported that the THC content of sinsemilla has remained stable in England over the past 11 years, the decreasing availability of resin (the only reliable source of CBD) has reduced the overall proportion of CBD within the cannabis market. Moreover, our findings indicate that, in the few available resin samples, the average THC content has significantly increased whereas average CBD content has decreased compared to those of samples analyzed in 2005,[9] pointing at a cannabis street market dominated by high-potency varieties.

Self-titration, or smoking less when using high--potency cannabis, has been suggested by some as a method for potentially counteracting the impact of high-potency cannabis use. Although this method may be used by experienced adult users, no published data suggest this approach is common among young adolescents, who are the most vulnerable group in terms of experiencing psychosis associated with cannabis use.[38]

Finally, data from the United States on the impact of widespread changes to cannabis legislation are becoming available. An article recently published by Hasin et al indicated that, in US states such has California that have passed medical marijuana laws, both an increased prevalence of illicit cannabis use and, more importantly, of cannabis use disorders has been noted. The authors concluded that, "*While medical marijuana may help some, cannabis-related health consequences associated with changes in state marijuana laws should receive consideration by health care professionals and the public.*"[39]

Recommendation

Although the potency and cannabinoid profile of sinsemilla appears to have remained unchanged over the past decade, the cannabinoid profile of resin circulating in England appears to be following the trend observed in France. This trend presents an increased risk of harm to those susceptible to the development of psychotic disorders following cannabis use. Future effort should be invested in a larger nationwide survey, which focuses on the distribution and cannabinoid content of resins and the cannabis oils and concentrates now starting to appear.

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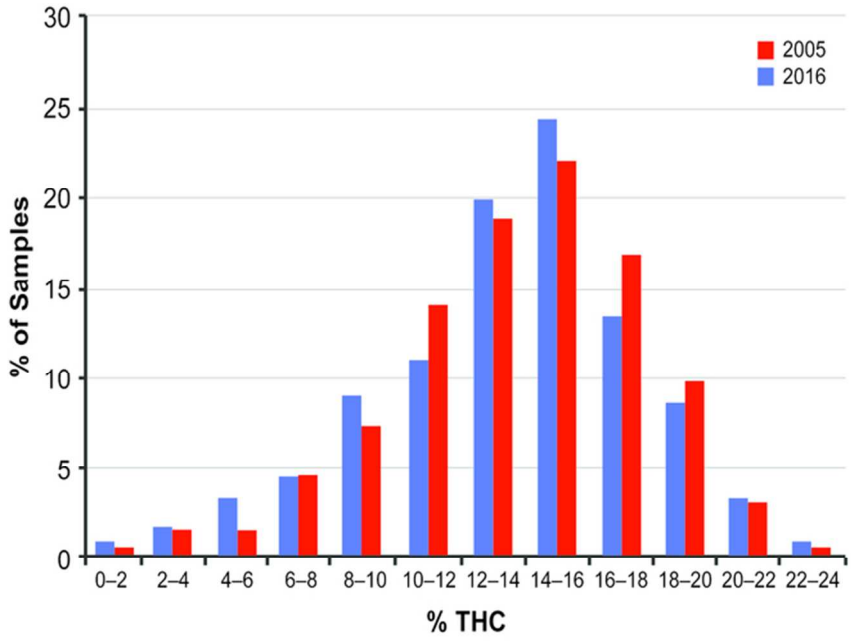

Figure 1. Range of sinsemilla THC contents in Derbyshire, Kent, London Metropolitan, Merseyside and Sussex in 2004/2005 (n = 247) and 2015/2016 (n = 400).

65x42mm (300 x 300 DPI)

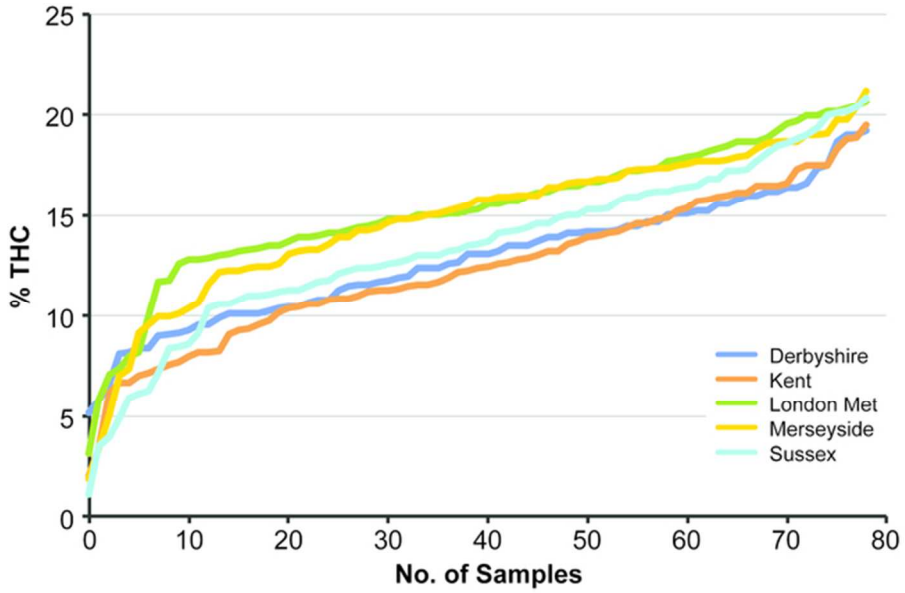

Figure 2. The %THC content of samples in each constabulary area, displayed in ascending potency.

60x36mm (300 x 300 DPI)

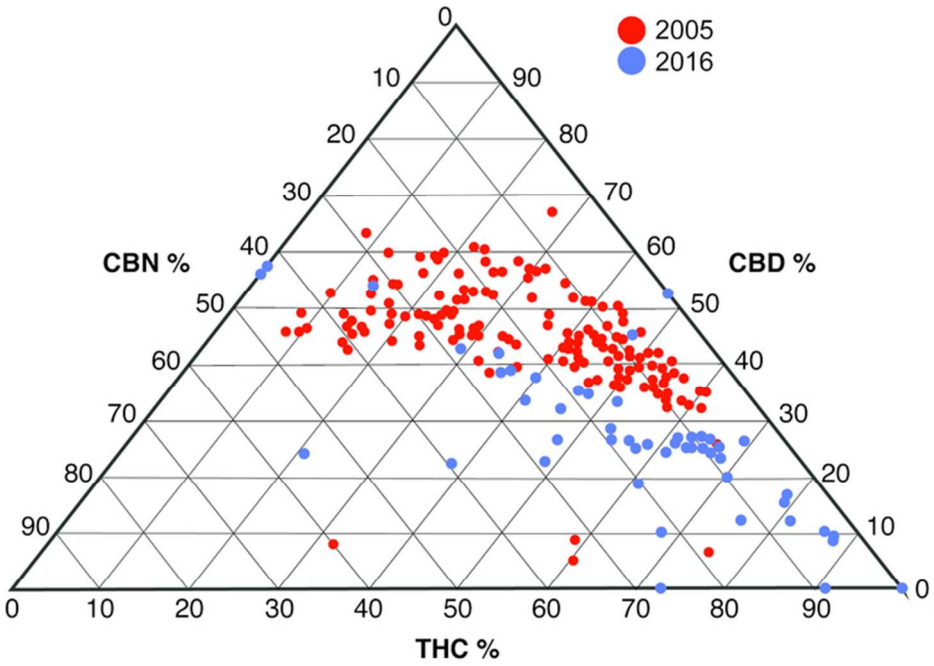

Figure 3. The varying THC:CBD:CBN ratios in illicit cannabis analyzed in 2005 and 2016.

68x45mm (300 x 300 DPI)

Figure 4. A selection of 15 illicit resin samples from 2016. A sample made on a police drug expert witness training event (bottom right) is included for comparison. Samples are shown in order of increasing THC content from top left to bottom right.

207x191mm (300 x 300 DPI)

Table 1. The Agilent 7890A Sample Preparation Program

	Rate °C/min	Value °C	Hold Time (min)	Run time (min)
(Initial)		60	3	2
Ramp 1	35	200	0	6
Ramp 2	5	250	5	21
Ramp 3	100	320	3.3	25

Table 2. Sample number in each constabulary region in each of three studies, 2005, 2008, and 2016.

		No. (% of Total)					
Year	**Type**	**London**	**Kent**	**Sussex**	**Merseyside**	**Derbyshire**	**Total**
2016	Sinsemilla	349 (95.9)	309 (94.5)	90 (85.7)	81 (87.1)	100 (96.2)	929 (93.6)
	Traditional	5 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	6 (0.6)
	Resin	10 (2.7)	18 (5.5)	15 (14.3)	12 (12.9)	3 (2.9)	58 (5.8)
	Total	364	327†	105	93	104	993†
2008	Sinsemilla	255 (93.1)	96 (82.8)	113 (80.7)	182 (82.0)	62 (83.8)	708 (84.5)
	Traditional	11 (4.0)	2 (1.7)	1 (0.7)	0 (0.0)	0 (0.0)	14 (1.3)
	Resin	8 (2.9)	18 (15.5)	26 (18.6)	40 (18.0)	12 (16.2)	104 (14.2)
	Total	274	116	140	222	74	826
2005*	Sinsemilla	96 (61.0)	58 (41.8)	34 (65.4)	44 (-)	15 (34.1)	247 (50.6)
	Traditional	30 (18.9)	0 (0.0)	3 (5.6)	1 (-)	1 (2.3)	35 (6.7)
	Resin	32 (20.1)	85 (59.4)	15 (28.8)	9 (-)	28 (63.6)	169 (42.7)

	Total	158	143‡	52	54	44	451‡

* Resin samples in Merseyside in 2005 were latterly added. True proportion would have been higher.

† In addition to the totals shown in 2016, there were 2 trichome resin powders from Kent.

‡ In addition to the totals shown in 2005, there was 1 trichome resin powder from Kent.

Table 2. Comparison of THC, CBD and CBN contents (% w/w) of the range of resin samples within the potency study, illustrated in Figure 4.

Sample Number	%THC	%CBD	%CBN
1	0.0	0.0	0.0
2	0.4	0.5	0.3
3	1.6	1.8	4.2
4	2.2	0.9	0.4
5	3.6	1.1	1.2
6	3.9	2.9	1.5
7	4.0	2.6	1.2
8	5.6	2.5	1.5
9	10.6	4.2	1.9
10	10.8	1.8	1.7
11	11.8	11.3	1.9
12	12.1	4.4	1.7
13	15.5	2.3	1.2
14	25.7	2.8	0.9
15	29.3	3.0	1.1
16*	41.0	0.6	1.0

* All samples are from the 2016 potency study, except sample 16, which was made during a police drug expert training event.

Figure 1. Range of sinsemilla THC contents in Derbyshire, Kent, London Metropolitan, Merseyside and Sussex in 2004/2005 (n = 247) and 2015/2016 (n = 400).

Figure 2. The %THC content of sinsemilla samples in each constabulary area, displayed in ascending potency.

Figure 3. The varying THC:CBD:CBN ratios in illicit cannabis analyzed in 2005 and 2016.

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